



## Understanding The 505(b)(2) Approval Pathway

*A Q&A with Ken Phelps, President and CEO, Camargo Pharmaceutical Services*

By the time he founded Camargo Pharmaceutical Services in 2003, Ken Phelps had already amassed more than 30 years of experience in the health science and services industry. With a broad background in drug development, specifically the 505(b)(2) regulatory approval pathway, Phelps has aided in the successful FDA approval of numerous compounds. Today, his company provides a full spectrum of drug development capabilities, from pre-clinical feasibility assessments to clinical program development to regulatory review and submission.



In this Q&A, Phelps discusses 505(b)(2) — how it differs from 505(b)(1), its myriad of benefits, its continuing evolution, and its current and future impact on drug development.

---

**Can you please give a brief introduction to Camargo Pharmaceutical Services, for readers who may not be familiar with your company?**

Camargo Pharmaceutical Services is a full-service drug development company, founded in 2003 to serve smaller, emerging, virtual companies, predominantly in the 505(b)(2) drug development process. Camargo works with companies to develop comprehensive programs, managing every facet of the plan from formulation and testing the drug product, to conducting clinical studies and FDA application submissions.

**Speaking of 505(b)(2), what are the differences between 505(b)(1) and 505(b)(2) submissions?**

The 505(b)(1) process is what the industry is familiar with — it is executed for new drugs like those discovered by big pharma. The 505(b)(2) process takes drugs that have already been approved and makes small modifications to them, often significantly advancing the medication for the patients' benefit.

**What is a bridging study, and why is it pivotal in the difference between 505(b)(1) and 505(b)(2) submissions?**

A Phase I bridging study is used to compare the systemic levels of the drug(s) between the proposed drug product and the reference product. Done properly, a bridging study allows a company to reference the safety and efficacy information that is already known for the original drug.

**This year marks the sixth anniversary of the FDA clearing the legal challenges to 505(b)(2) submissions. What impact do you feel this decision has made?**

In fiscal year 2006, approximately 20% of new drugs were approved through the 505(b)(2) process. In 2007, the number was about 43%. In 2008, more than half of the new drugs approved in the United States were based on the 505(b)(2) process. Looking at the number of Investigational New Drug Applications (INDs) we are filing, we expect that by 2012, the percentage of 505(b)(2) approvals will be greater than 90%.

**What role does Camargo play in the 505(b)(2) process?**

The 505(b)(2) process is relatively new. It is still evolving at the FDA — they are continually evaluating procedures and the requirements for approval. Camargo is at the FDA three, five, or even more times a month doing 505(b)(2) drug processes, so we understand what the FDA requires for approval.

Moreover, the agency relies on public information for many studies. Our scientists review this information and positioning so the FDA accepts it, in lieu of studies that the sponsors may have to run themselves.

**Is this approach the equivalent to drug repositioning?**

No, the drug repositioning process is where big pharma takes drugs that failed clinical programs. They make changes in the endpoints of their studies or make changes to the molecule itself in order to get approval.

**How do your study designs streamline the overall clinical drug development plan?**

Camargo takes advantage of the known safety and efficacy of the active pharmaceutical ingredient (API) when designing studies. This allows some studies to be performed in parallel and some studies to be combined, which ultimately results in fewer, faster, and cheaper studies than traditional drug development.

**What are the benefits of using the 505(b)(2) process?**

The 505(b)(2) process is relatively low risk because the drug has already been proven to be safe. It is low

cost because there are fewer studies. It is also faster due to fewer studies, and, if done right, a drug can make it to market in as little as 3 years. It is very important in the economic climate today that our clients quickly get these drugs on the market.

**How does CMC (chemistry, manufacturing, and controls) play a role in the development program for a 505(b)(2) submission?**

During the 505(b)(2) drug development process we often change the formulation, components, or API. The impact of any of these changes must be evaluated for impact on the safety and efficacy of the proposed drug product. A review of the evolution of the formulation and the data supporting the comparability of the different formulations form the basis for the Pharmaceutical Development section of the eCTD (electronic common technical document). A CMC bridging study can accomplish these goals.

Taking care to review the implications of changes during the development process and incorporating prudent comparability protocols at the right point in the program can answer a lot of questions, and provide a coherent and approvable pharmaceutical development summary for the proposed drug product.

**Are stability studies or clinical studies the limiting factor on FDA submissions for 505(b)(2)?**

All too often, stability studies are the rate-limiting step. The clinical program for many 505(b)(2) drug development programs is often ahead of the formulation development, analytical methods development, and scale-up activities. For this reason, some sponsors accept the risk and scale up early in Phase I.